BIOCHEMICAL CHARACTERIZATION OF WARM ISCHEMIC INJURY TO VALVE LEAFLET FIBROBLASTS IN A PORCINE MODEL USING PROTON (^{1}H) MAGNETIC RESONANCE SPECTROSCOPY.

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Tissue harvesting of allograft valves involves variable warm ischemia times (WIT). We assessed the time course of injury to leaflet (Lft) fibroblasts by proton magnetic resonance spectroscopy of lactate (Lac) accumulation in 102 semilunar valves. Lft's were analyzed over WIT's from 40 min to 36 hrs. Spectra were generated using an SIS Spectrometer (4.7 Tesla, spectral width of 4 kHz, acquisition time of 0.5 sec and recycle time of 2 sec with 64 acquisitions). Absolute concentrations of Lac were derived by referencing the peak areas to a known standard. A radiolabeled proline incubation assay was used to measure protein synthesis. Proline incorporation (n=54) at WIT=6 hrs was 1.28±0.11 nmol/mg and decreased at WIT=24 hrs to a passive absorption level of 0.39±0.023 nmol/mg (p<0.001). Proline data demonstrates a cessation of structural protein synthesis by 24 hrs of WIT. Lac accumulates from the second hr of ischemia to 36 hrs. Although switching from aerobic to anaerobic metabolism within the first two hrs of WIT, leaflet fibroblasts exhibit remarkable resistance to hypoxia. This may represent an extended "window" for harvesting "viable" fresh tissue.

WIT(hrs)	LAC(umol/mg wet wt.)
0.66	4.45±2.66
1	12.77±11.53(p<0.20)
2	18.09±8.75 (p<0.05)
4	13.19±4.76 (p<0.05)
6	30.09±19.52(p<0.001)
12	31.84±11.42(p<0.001)
24	49.95±15.53(p<0.001)
36	96.96±24.95(p<0.001)

TRENDS IN THE SURGICAL MANAGEMENT OF ISCHEMIC MITRAL REGURGITATION: EFFECTS OF MITRAL VALVE REPAIR

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Moderate to severe mitral regurgitation precipitated by acute myocardial infarction (IMR) is an uncommon manifestation of coronary artery disease that has been associated with suboptimal surgical results. From Jan. 1981-Dec. 1988, 211 patients with IMR were treated surgically, 129 with coronary bypass (CAB) only (GpI), and 82 with a mitral valve procedure ± CAB(GpII). GpI had worse angina (p=.01) and more extensive coronary disease (p=.001), whereas GpII had more severe regurgitation and congestive heart failure (both p<.001). Two-thirds of both groups required emergency operation from the CCU. Multivariate logistic regression revealed 1) requirement for valve procedure (p<.0002), 2) year of therapy (p=.003), 3) number of comorbid disorders (p=.008), and necessity for CCU management (p=.025) as predictors of hospital mortality. Predicted mortality for GpI in 1981 was 23% and fell to 3% by 1988; mortality for GpII was 56% in 1981 and fell to 18% in 1988. Severity of patient illness and mortality for mitral valve replacement (avg. 45%) did not change significantly over time. The increasing application of mitral valve repair (avg. mortality 18%) to two-thirds of GpII patients over the past 4 years seems to be the factor primarily associated with falling mortality in GpII, despite similar baseline characteristics between repair and replacement patients. Intraoperative transesophageal colorflow mapping and better patient selection for CAB may account for improving mortality in GpI. Surgical results in IMR are now approaching those observed in non-IMR patients because of improved patient selection and increasing use of valve reconstruction.

OPERATIONS FOR HYPERTROPHIC SUBAORTIC STENOSIS ASSOCIATED WITH MITRAL INSUFFIENCY

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Forty-two consecutive patients with hypertrophic subaortic stenosis (IHSS) and moderate to severe mitral insufficiency were operated on from 1972-88. Methods of relief of left ventricular (LV) outflow obstruction were septal myectomy/myotomy (n=34), mitral valve replacement (MVR) (n=5), and myectomy/myotomy plus MVR (n=3). Concomitant procedures included CABG (n=4), and aortic valve replacement (n=2) or repair (n=2). LV outflow gradient decreased from 79+38 to 11+10. There were five hospital deaths (12%), all in patients older than 65, and no mortality in the 28 younger patients (p<0.001). Double sampling dye curves were performed immediately after cardiopulmonary bypass in 24 who underwent myectomy alone. Only two showed early dye appearance in the left atrium as evidence of significant (20-25%) mitral insufficiency. Both had destruction of valve leaflets by bacterial endocarditis, one died, and the other underwent successful valve replacement. Followup ranged from 0.5-9 years (mean 4.4), and five years actuarial survival including hospital mortality was 76%. Preoperative symptoms were relieved in 19 of 28 (68%) with dyspnea, 20 of 24 (63%) with angina, and 7 of 10 (70%) with syncope. Mitral insufficiency in most patients with IHSS may be alleviated safely by myotomy/myectomy alone.

Monday, March 19, 1990
2:00PM–3:30PM, Room 23
Ischemic Heart Disease: Basic and Clinical Mechanisms

EVIDENCE AGAINST SIGNIFICANT ALPHA2 POSTSYNAPTIC CORONARY VASOCONSTRICTION IN RESTING MAN.

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Alpha2 adrenoceptor-mediated coronary vasoconstriction occurs in dogs. To assess whether or not alpha2 postjunctional adrenoceptors affect resting coronary blood flow we studied 6 human subjects with angiographically normal coronary arteries. Regional coronary blood velocity was measured during cardiac catheterization with a subselective 3F intracoronary Doppler Catheter. Epicardial coronary artery diameter was measured by automated analysis of digital coronary arteriograms. Beta-blockade (propranolol 0.1 mg/kg i.v.) was administered in order to avoid prejunctional release of Norepinephrine. Regional alpha2-adrenoceptor blockade was produced by intracoronary infusion of Yohimbine (0.2 ug/Kg/min (Y1), 1 ug/Kg/min (Y2), 2 ug/Kg/min (Y3). Y3 is a dose which completely blocks specific alpha2 adrenoceptor agonist activity in dogs. Each dose over 4'.

	BASE	Y1	Y2	Y3
Flow (ml/min)	46±19	48±19	47±24	50±22
Velocity (cm/sec)	7±2	7±2	7±3	7±3
HR (bpm)	67±7	68±8	67±8	68±7

The intracoronary infusion of Yohimbine did not change aortic pressure. Additionally, no change in epicardial coronary artery diameter were observed. These data provide the first evidence in man that postsynaptic alpha2 adrenoceptor-mediated coronary tone is negligible under resting conditions.